

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently amended) A method of selecting phage that encode a target binding protein from a plurality of display phage, the method comprising:
  - a) forming a mixture comprising a plurality of diverse display phage, a target, and a support, wherein each phage of the plurality displays a heterologous protein component on its surface and each phage includes a nucleic acid encoding the heterologous protein component, the heterologous protein component being a member of a set of diverse protein components;
  - b) forming phage immobilized target complexes phage immobilized to the support, each of which comprises a phage from the plurality which binds the target and the target immobilized to the support;
  - c) separating phage that do not bind to the target from the phage-immobilized phage immobilized to the support via binding to the target complexes;
  - d) contacting host cells with the phage-immobilized phage immobilized to the support target complexes so that the host cells are infected by phage from the phage-immobilized phage immobilized to the support target complexes to yield a first population of infected cells;
  - e) producing replicate phage from the infected cells in the presence of the target immobilized to the support, thereby forming replicate phage-immobilized phage immobilized to the support via binding to the target complexes;

- f) separating replicate phage that do not bind to the target from the replicate phage-immobilized phage immobilized to the support target complexes; and
- g) contacting host cells with the replicate phage-immobilized phage immobilized to the support target complexes so that host cells are infected with the replicate phage immobilized to the support to yield a second population of infected cells.

2. (Original) The method of claim 1 further comprising recovering the second population of infected cells.

3. (Original) The method of claim 1 further comprising recovering phage produced by the second population of infected cells.

4. (Original) The method of claim 1 further comprising repeating steps e) to g) at least once.

5. (Original) The method of claim 1 wherein steps a) to g) are conducted in the same vessel.

6. (Original) The method of claim 1 wherein steps d) to e) occur in the same vessel.

7. (Original) The method of claim 1 wherein steps b) to g) are conducted without addition of the target.

8. (Original) The method of claim 1 wherein step e) comprises supplying the mixture in which the replicate phage are produced with an additional amount of the target.

9. (Original) The method of claim 1 wherein, during step e), fewer than 5000 progeny phage are produced for each phage that infects one of the host cells.

10. (Original) The method of claim 1 wherein step e) is completed in less than 4 hours.

11. (Original) The method of claim 1 wherein, during step e), the host cells divide less than seven times.

12. (Original) The method of claim 1 wherein time between the contacting d) and the separating f) is less than 240 minutes.

13. (Original) The method of claim 1 wherein the diverse set of protein components consists of between  $10^3$  and  $10^{12}$  different protein components.

14. (Original) The method of claim 1 wherein the producing comprises a change in temperature.

15. (Original) The method of claim 1 wherein each diverse phage of the plurality comprises genes sufficient for phage replication in a host cell.

16. (Currently amended) The method of claim 1 wherein each diverse phage of the plurality is a phagemid, and the step e) producing replicate phage from the infected cells in the presence of the target immobilized to the support, thereby forming replicate phage-immobilized phage immobilized to the support via binding to the target complexes comprises contacting helper phage to the host cells.

17. (Currently amended) The method of claim 1 wherein a competing ligand is present during an interval of the step e) producing replicate phage from the infected cells in the presence of the target immobilized to the support, thereby forming replicate phage-immobilized phage immobilized to the support via binding to the target complexes.

18. (Original) The method of claim 1 wherein during step e) and/or g) the host cells are cells of a mutator strain.

19. (Canceled)

20. (Previously presented) A method of identifying members of a bacteriophage library that have a desired binding property, the method comprising:

(a) providing a bacteriophage library that comprises a plurality of bacteriophage members;

(b) selecting a subset of the bacteriophage members;

(c) infecting host cells with the members of the subset;

(d) amplifying members of the subset under at least one of the following conditions:

(1) fewer than 5000 progeny phage are produced for each phage member selected in step (b);

(2) less than 4 hours elapses; and

(3) the host cells divide less than 6 times; and

(e) selecting a subset of the amplified members, thereby identifying the desired members of the bacteriophage library.

21. (Original) The method of claim 20 wherein the amplifying (d) occurs in the presence of a target, and step (e) comprises selecting amplified members that bind to the target.

22. (Original) The method of claim 21 wherein the target is a compound that is immobilized during the amplifying (d).

23. (Original) The method of claim 22 wherein step (b) comprises contacting the bacteriophage library to a target and a solid support, immobilizing members of the library that bind to the target, and separating members of the library that bind to the target from members of the library that do not bind to the target.

24. (Currently amended) A method of selecting a nucleic acid that encodes a binding protein from a library of display phage, the method comprising:

a) providing a library of phage that each have a heterologous protein component that is diverse among the phage of the plurality, physically attached to the phage, and accessible;

b) contacting phage of the library to a target;

c) performing one or more cycles of:

i) forming phage-immobilized target complexes phage immobilized to a support, each of which comprises (1) a phage that binds to the target by its heterologous protein component and (2) the target immobilized to a support,

ii) separating phage that do not bind to the target from the phage-immobilized phage immobilized to the support via binding to the target complexes,

iii) contacting phage from the phage immobilized the phage immobilized to the support target complexes with host cells so that the host cells are infected by the phage from the immobilized to the support phage-immobilized target complexes, and

iv) producing phage from the infected cells in the presence of the target, the produced phage being replicates of phage that bind to the target; and

d) recovering the nucleic acid encoding the heterologous protein component of one or more produced phage that bind to the target, thereby selecting a nucleic acid that encodes a binding protein for the target.

25. (Original) The method of claim 24 wherein conditions of the separating in step ii) vary in stringency during the cycles.

26. (Original) The method of claim 24 wherein at least two cycles are performed.

27. (Original) The method of claim 26 wherein at least three cycles are performed.

28. (Original) The method of claim 24 wherein each cycle is completed in less than 8 hours.

29. (New) A method comprising: maintaining a plurality of host cells in the presence of a target compound, each host cell containing a nucleic acid encoding a candidate protein that is attachable a bacteriophage particle and that varies among the plurality of host cells, the maintaining being under conditions wherein the host cells of the plurality produce bacteriophage particles that include the attached candidate proteins; and immobilizing a subset of the bacteriophage particles, wherein the particles of the subset include attached candidate proteins that bind to the target compound.

30. (New) A method of amplifying a plurality of display library members, the method comprising: amplifying a plurality of display library members in the presence of a target to yield a population of amplified display library members, wherein during or after the amplifying, at least a subset of the amplified display library members physically interact with the target.

31. (New) A method of selecting members having a desired binding property from a bacteriophage library, the method comprising: providing a first plurality of diverse bacteriophage, wherein the first plurality is characterized by a first titre; selecting a subset of the first plurality, wherein the subset is less than 0.01% of the first plurality; amplifying members of the subset to provide amplified members; and contacting a second plurality of bacteriophage to a target, wherein the second plurality is characterized by a second titre that is less than one-tenth of the first titre.

32. (New) A method of amplifying a display phage, the method comprising: immobilizing phage that display a protein entity on their surface on a support that includes a target; contacting a host cell to the support under conditions that allow the immobilized phage to infect the host cell; and culturing the host cell in the presence of the support under

conditions that enable production of replicates of the immobilized phage, thereby amplifying the immobilized phage.

33. (New) A method of selecting a display library member, the method comprising: amplifying a display library member in a defined nutritive medium that supports growth of a microorganism; and binding the amplified display library member to a target in the defined nutritive medium.

34. (New) A library of display phage comprising: a plurality of diverse display phage derived from a plurality of input display phage, the library consisting of fewer than 10,000 replicates of each input display phage, and that is isolated by a method comprising providing a plurality of input display phage that each interact with a target, and amplifying each of the input display phage under at least one of the following conditions: (1) fewer than 5000, 1000, 500, or 200 progeny phage are produced for each input phage; (2) less than 4, 3, 2, 1, 0.8 hours elapses; and (3) an antibiotic whose resistance is encoded by a nucleic acid within each bacteriophage member is absent or present.

35. (New) A method of processing a plurality of display phage, the method comprising: (1) contacting a plurality of diverse display phage to a target; (2) separating phage that bind to the target from unbound phage; and (3) one or more cycles that include:

- a. infecting host cells with the phage that bind to the target in a first vessel;
- b. transferring the host cells to a second vessel,
- c. producing replicate phage from the infected cells in the presence of the target in the second vessel;
- d. separating phage that bind the target from the unbound phage and infected hosts cells;
- e. repeating a. to d. one or more times.

36. (New) A method of selecting a binding protein, the method comprising: providing complexes including a target and bacteriophage particles that each display a

heterologous protein; contacting the complexes with a given ligand that binds to a discrete epitope of the target under conditions that cause dissociation of one or more of the bacteriophage particles; infecting host cells with the one or more dissociated bacteriophage particles; and maintaining the host cells in the presence of the target under conditions whereby replicates of the one or more dissociated bacteriophage particles are produced.

37. (New) A method of selecting a subset of bacteriophage particles, the method comprising: maintaining bacterial host cells in the presence of a target-presenting cell that includes a target compound accessible to medium surrounding the cell, the host cells containing nucleic acid encoding a plurality of different candidate proteins that are attachable a bacteriophage particle, the maintaining being under conditions wherein the bacterial host cells produce bacteriophage particles that include the attached candidate proteins; and separating a subset of the bacteriophage particles that bind to the target-presenting cells from the bacteriophage particles produced by the bacterial host cells.

38. (New) A method for selecting a desired protein or peptide from a bacteriophage library comprising: (a) providing a bacteriophage library that includes a plurality of bacteriophage members; (b) selecting a subset of the bacteriophage members; (c) infecting host cells with the members of the subset; (d) amplifying members of the subset, wherein (i) during amplifying, fewer than 5000, 4000, 2000, 1000, 700, 500, or 300 progeny phage are produced for each phage that infects one of the host cells; (ii) the amplifying is completed in less than 4, 3, 2 1.5, 1, or 0.5 hours; (iii) during the amplifying, the host cells divide less than seven, six, five, four or three times; and (iv) during the amplifying, an antibiotic whose resistance is encoded by a nucleic acid within each phage is present or absent; and (e) selecting a subset of the amplified members, thereby selecting members having desired protein or peptide from the bacteriophage library.